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Assessment of Clinical and Biochemical Profile of Prediabetic Subject in Bangladesh, Attending in BIRDEM and results of Intervention by Lifestyle Modification, Metformin, and DPP4 Inhibitor

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Abstract: *Prediabetes is a reversible condition that increases an individual's risk for progress to diabetes.The aim of the study is to assess prediabetic profile before and after life style modification only, lifestyle with metformin and lifestyle with DPP-4 inhibitor. This prospective interventional study was carried out at Endocrine OPD of BIRDEM general hospital over the period of 12(twelve) months from Jan 2017 to Dec 2017. The subjects who were screened for DM by OGTT according to WHO criteria, were approach whose value are in the range of IGT, IFG or combined. The subjects are randomly selected as first person in group A (lifestyle only), second person in group B (lifestyle with metformin) and third person in group C (lifestyle with DPP4i). Drug compliance are 84%, 88%, and 76% and drop out are 16%, 12%, and 26% in lifestyle only, lifestyle plus Metformin, and lifestyle plus DPP4i respectively. Mean drop out is 18% and most of them are due to non adherence to study protocol and drug adverse effect. In Group A 50 subjects were advised with lifestyle, 42 were follow up with the results showed that highly significant change in BMI (p-0.002), Fasting (p-0.001) & 2 hr plasma glucose level (p-0.003) serum triglyceride level (p-0.012) and reduced HbA1c level (p-0.0075) respectively, reduction rate of DM is 43%. There is no effect on systolic and diastolic blood pressure and also on total cholesterol, HDL and LDL. In Group B 50 subjects were advised with lifestyle plus metformin, 44 were follow up with the results showed that significant change in BMI (p-0.003) Fasting (p-0.0001) & 2 hr plasma glucose level (p-0.0001) serum triglyceride level (p-0.04) and reduced HbA1c level (p-0.0003) respectively and reduction rate of DM is 58%. There is no effects on systolic & diastolic blood pressure and also in HDL, LDL and total cholesterol level. In Group C 50 subjects were advised with lifestyle plus DPP4i, 37 were follow up with the results showed that significantly change in BMI (p-0.05) Fasting (p-0.0001) & 2 hr plasma glucose level (p-0.0001) serum triglyceride level Fasting (p-0.03) and reduced HbA1c level (p-0.0004) respectively and reduction rate of DM is 43%. There is no effects on systolic & diastolic blood pressure and also in HDL, LDL and total cholesterol level. There is no significant outcome difference in BMI in between B & C group but outcome difference in between A vs. B (P-0.05) and A vs. C group (P-0.04).There is no significant outcome difference in SBP, DBP, HbA1c and fasting blood sugar in between three intervention group. But more mean changed in 2hrs after blood sugar level in group A vs. group B (p-0.02) and B vs. C group (p-0.04). Mean changed in fasting blood sugar and 2 hrs after blood sugar, the outcome is same in between A and C group (p-0.73). There is no outcome difference in LDL, HDL and total cholesterol level in between intervention group but there is significant outcome difference in TG level in A vs. B (P-0.04), B vs. C group (P-0.05) but no significant difference in A vs. C group (p-0.24). Nausea (10%), abdominal distension (16%), diarrhea (12%) were the common adverse effects lifestyle plus metformin group where as nausea (8%), headache (10%) and abdominal discomfort (10%) were the common adverse effect in lifestyle plus DPP4i intervention group. No serious adverse effects were reported in the study group. No significant difference in DM reduction among the three group is seen.This study provides evidence that type 2 diabetes can be prevented by significant improvement in clinical and biochemical profile with metformin and DPP4 inhibitors along with lifestyle intervention.*

Keyword: *Prediabetic, Metabolic syndrome, DPP4 inhibitor, Metformin*

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I. Introduction

Prediabetes is a metabolic condition characterized by insulin resistance and primary or secondary beta-cell dysfunction, which increases the risk of type 2 DM.[1] The American Diabetes Association defines prediabetes as either impaired glucose tolerance (IGT; 2-hour postprandial glucose of 7.8-11.0 mmol/L) or impaired fasting blood glucose (FBG; value of 5.6-6.9 mmol/L), or both.[2] Risk factors for prediabetes include the family history of diabetes, excess body weight (particularly abdominal adiposity), age >45 years, gestational diabetes, high birth weight children, certain ethnic groups, hypertension, and physical inactivity.[3] Glucose levels above the normal, but below the threshold diagnostic for diabetes, are associated with a substantially increased risk of developing cardiovascular disease and death.[4]

Prediabetes is a condition in which individuals have blood glucose levels higher than normal but not high enough to be classified as diabetes. People with prediabetes have an increased risk of Type 2 diabetes and CVD. An estimated 34% of adults have prediabetes.[5] Prediabetes is now recognized as a reversible condition that increases an individual's risk for development of diabetes. Lifestyle risk factors for prediabetes include overweight and physical inactivity.

Increasing awareness and risk stratification of individuals with prediabetes may help physicians understand potential interventions that may help decrease the percentage of patients in their panels in whom diabetes develops. If untreated, 37% of the individuals with prediabetes may have diabetes in 4 years.[5] Lifestyle intervention may decrease the percentage of prediabetic patients in whom diabetes develops to 20%.

Investment in a diabetes prevention program now may have a substantial return on investment in the future and help prevent a preventable disease. The primary aim of lifestyle interventions, treatment with metformin and DPP-4 inhibitor are to prevent diabetes and its complications by targeting obesity and physical inactivity, improvement of residual beta cell function. The goal for prediabetes treatment should be to normalize blood glucose levels. Strategies targeting interventions aimed at the entire population at risk of prediabetes can make health care more affordable, prevent a preventable disease, and save lives. This study aims to determine the clinical and biochemical profile of prediabetic subjects and results of intervention with lifestyle modification, metformin and DPP-4 inhibitors in preventing the progression from prediabetes to type 2 DM, and thus may add to the armamentarium of agents utilized for the management of prediabetes.

II. Materials and Method

It is an interventional study carried out at Endocrine OPD of BIRDEM general hospital. Study was carried over the period of 12 (twelve) months, dated from January 2017 to December 2017 then 3 (three) months extended for data collection. Study population was consisting of subjects who came for screening diabetes mellitus. Those populations were approaches whose value are in the range of IGT, IFG or combined. From the previous study it is regarded as 22% (0.22) of Bangladeshi adult population had prediabetes.[6] So Due to time constrain total 150 subjects were taken, 50 subjects in each group. **Group-A** who received intervention by lifestyle modification only; **Group-B** of which was followed lifestyle modification with metformin, and **Group-C** who received lifestyle modification with DPP-4 inhibitor. The primary end point was the progression from prediabetes to type 2 DM at the end of the 1 year study period. Purposive type of consecutive random sampling of the prediabetic subjects who were willing to participate. 1st person was included in Group A, 2nd person in Group B and 3rd person in Group C and so on. Subjects with impaired glucose tolerance as defined by American Diabetes Association, impaired fasting glucose of 6.1 – 6.9 mmol/l or 110 – 125 mg/dl, impaired glucose tolerance (2-hour postprandial glucose of 7.8–11.0 mmol/L or 140-199 mg/dl), ge ≥ 18 years, no history of liver disease or renal disease**, w**illing to give consent were included in the study and subjects having iImpaired liver function tests, cardiac failure or history of congestive heart failure, medication that may affect insulin resistance (e.g. thiazide diuretics)**, a** ny morbidity that contraindicates exercise **, p** regnancy history of GDM **and h** istory of hypersensitivity reaction to DPP-4 such as anaphylaxis or angioedema were excluded from the study.

Visit 1 - Study Start

Subjects were briefed about the study and invited to participate. Thereafter, informed consent was obtained. Screening tests that had already done by the patient was search to determine if subjects meet the criteria for inclusion in the study(e.g. liver function tests [LFTs], renal function test, HbA1c, OGTT, fasting lipid profile). History taking including drug history, physical examination also had done side by side. Subjects meeting the inclusion criteria were invited to join the study. Patients unable or unwilling to return to their initial referring site were treated at the study sites. All subjects were given dietary advice from dietary chart according

to his body weight and a standard exercise protocol from the Diabetic Education Department of BIRDEM. Subjects were randomized to either lifestyle modification only (group A) or lifestyle with metformin (500 mg open level drug) twice daily (group B) or lifestyle with Vildagliptin(50 mg open level drugs) once dailyas DPP4 inhibitor (group C).

Visit 2 – Two weeks later

Measures for determining safety and drug side effect were examined. 5 subjects in group B and 3 subject in group C were complaints of mild abdominal discomfort but they continue with adequate reassurance.Lifestyle modification (LSM) advice was reinforced.

Visit 3 and subsequent follow up as required

Every time subjects visited for any problem regarding present condition or condition other than that was taken in consideration and managed accordingly as a part of follow up of the patient and record any side effect of the drug, the problem in following up the dietary chart or performing the physical exercise as needed. All the follow up was recorded in the case record sheet. The patient who could not come physically for any problem arising during the study period was contacted over mobile phone and advice was given as needed.

Visits 4 – One year later

During the last visit after one year, measures of glycemic status(FBS, 2HAB, HbA1c), liver function test, renal function test, anthropometric measures, lipid profile, safety data (biochemical and clinical) were assessed. Primary endpoints include the number of subjects progressing from prediabetes to type 2 DM. Secondary endpoints include dyslipidaemia, alteration of renal function test, liver function test, full blood count, OGTT, weight and other anthropometric parameters with blood pressure without preceded to T2DM.

Rescue visit: Any adverse event occurring during the whole study period, patients came for consultation and possible management.

After editing and coding, the coded data was directly entered into the computer by using SPSS software, version 20.0). Data cleaning validation and analysis were performed using the SPSS software. Categorical data were presented as frequency, percentage and the continuous variable were expressed as mean±SD (standard deviation). An independent sample Student's t-test was used for comparison of means of continuous variables with normal or approximately normal distributions. The Chi-square test was used to analyze discrete variables. The statistical significance threshold was set to $p \leq 0.05$ (two-tailed). The confidence interval was set at 95% level. Determinants of adherence to medication were assessed by logistic regression analysis. Statistical significance was set at $p<0.05$.

III. Results And Observations

The observation and results have been shown in different tables and figures.

Table-1: Baseline characteristic of the prediabetic(IFG/IGT/IFG+IGT) **subjects**

Variable	Group A N=50 (LSM)	Group B N=50 (LSM + Met)	Group C N=50 (LSM + DPP4i)	Difference in between group
Age (years)	44.5 ± 6.4 (30-48)	45.2 ± 5.9 (32-49)	44.6 ± 6.1 (32-50)	0.827 NS
BMI	24.1 ±6.7 (22-31)	24.5 ± 7.1 (22-32)	24.0 ± 6.8 (21-31)	0.929 NS
Systolic blood pressure (mmHg)	124.0 ± 14.2 (110-130)	125.2 ± 13.7 (112-138)	123.8 ± 12.6 (115-135)	0.855 NS
Diastolic blood pressure (mmHg)	75.1 ± 10 (65-75)	76.0 ± 11.4 (65-78)	78.1 ± 12.5 (65-90)	0.466 NS
Fasting plasma glucose (mg/dl)	109 ± 14 (95-120)	111 ± 13 (90-122)	110 ± 12 (94-124)	0.745 NS
2 hr after 75gm glucose(mg/dl)	159 ± 25 (140-190)	157 ± 26 (145-192)	156 ± 24 (143-188)	0.830 NS
Serum Total Cholesterol (mg/dl)	215 ± 37 (150-275)	210 ± 35 (156-246)	212 ± 30 (158-248)	0.944 NS
Serum Triglyceride (mg/dl)	154 ± 71 (140-250)	152 ± 59 (130-230)	156 ± 61 (135-245)	0.952 NS
Serum LDL (mg/dl)	95 ± 27 (50-145)	97 ± 30 (55-135)	93 ± 32 (60-125)	0.798 NS
Serum HDL (mg/dl)	46 ± 12 (25-55)	48 ± 13 (28-55)	47 ± 14 (30-57)	0.745 NS
HbA1c (%)	5.91±0.44 (5.2-6.3)	5.81±0.47 (5.1-6.2)	5.83±0.46 (5.1-6.3)	0.513 NS
Family History of DM	68.3%	69.4%	67.6%	NS

Note: Anova test was done. NS –Not significant

Table-1 shows the baseline characteristics of the patients before intervention with lifestyle or lifestyle with metformin and lifestyle with DPP4 inhibitors have no significant difference.

Table-2: Effects on lifestyle modification on prediabetic subjects after the end of the study (Group A)

Variable	Baseline N=50	End of the study N= 42	Mean change difference Confidence interval	P value
BMI	24.1 ±6.7	20.2 ± 5.8	2.000 (-0.064 to 4.064)	**0.002**
Systolic blood pressure (mmHg)	124.0 ± 14	123 ± 12	1 (-4.17 to 6.17)	0.70
Diastolic blood pressure (mmHg)	75 ± 10	74 ± 11	1 (-3.17 to 5.17)	0.63
Fasting plasma glucose (mg/dl)	109 ± 14	101 ± 10	8 (3.17 to 12.83)	**0.001**
2 hr after75gmglucose (mg/dl)	159 ± 25	140 ± 37	19 (6.47 to 31.53)	**0.003**
Serum Total Cholesterol (mg/dl)	215 ± 37	210 ± 35	1.00 (-12.50 to 14.50)	0.489
Serum Triglyceride (mg/dl)	154 ± 71	123 ± 49	19.00 (0.16 to 37.84)	0.**012**
Serum LDL (mg/dl)	95 ± 27	96 ± 28	-1.00 (-11.92 to 9.92)	0.85
Serum HDL (mg/dl)	46 ± 12	46 ± 10	0.00 (-4.38 to 4.38)	1.00
HbA1c (%)	5.91±0.44	5.7 ± 0.32	0.21 (0.0573 to 0.3627)	**0.0075**
Incidence of diabetes	0/50	3(6%)	-	-
Reduction rate of DM		43%		

Note: Paired t test was done

Table-2 shows that in Group A N=50 prediabetic subjects were advised for LSM, 42 were follow up at the end of study and found highly significant change in BMI (p-0.002) Fasting (p-0.001)& 2 hr plasma glucose level (p-0.003) serum triglyceride level (p-0.012)and reduced HbA1c level (p-0.0075) respectively. The progress to diabetes is only 6% and reduction rate of DM is 43% with lifestyle modification. There is no effect on systolic and diastolic blood pressure and also on total cholesterol, HDL and LDL.

Table-3: Effects on lifestyle modification with metformin on prediabeticsubjectsafter the end of the study (Group B)

Variable	Baseline N=50	End of the study N=44	Mean change difference Confidence interval	P value
BMI	24.5 ± 7.1	20.9 ± 4.8	3.9 (1.413 to 6.387)	**0.003**
Systolic blood pressure (mmHg)	125 ± 13	122 ± 12	3.0 (-1.97 to 7.97)	0.23
Diastolic blood pressure mmHg)	76.0 ± 11	74 ± 11	2.00 (-2.37 to 6.37)	0.36
Fasting plasma glucose (mg/dl)	111 ± 13	101± 08	10.00 (5.72 to 14.28)	**0.0001**
2 hr after75gmglucose (mg/dl)	157 ± 26	137 ± 35	24.00 (12.09 to 35.91)	**0.001**
Serum Total Cholesterol (mg/dl)	210 ± 35	209 ± 33	5 (-9.29 to 19.29)	0.88
Serum Triglyceride (mg/dl)	152 ± 59	133± 32	31 (6.79 to 55.21)	**0.04**
Serum LDL (mg/dl)	97 ± 30	95 ± 27	2.00 (-9.33 to 13.33)	0.72
Serum HDL (mg/dl)	48 ± 13	47 ± 11	1.00 (-3.78 to 5.78)	0.67
HbA1c (%)	5.81±0.47	5.5 ± 0.34	0.3300 (0.151 to 0.508)	**0.0003**
Incidence of diabetes	0/50	2(4%)	-	-
Reduction rate of DM		58%		

Note: Paired t test was done

Table-3 shows thatin Group B N=50 prediabetic subjects were advised for LSM+Met, 44 were follow up at the end of study and found highly significant change in BMI (p-0.003) Fasting (p-0.0001) & 2 hr plasma glucose level (p-0.001) serum triglyceride level (p-0.04) and reduced HbA1c level (p-0.0003) respectively. The

progress to diabetes is 4%and reduction rate of DM is 58%. There is no effect on systolic & diastolic blood pressure and also in HDL, LDL and total cholesterol level.

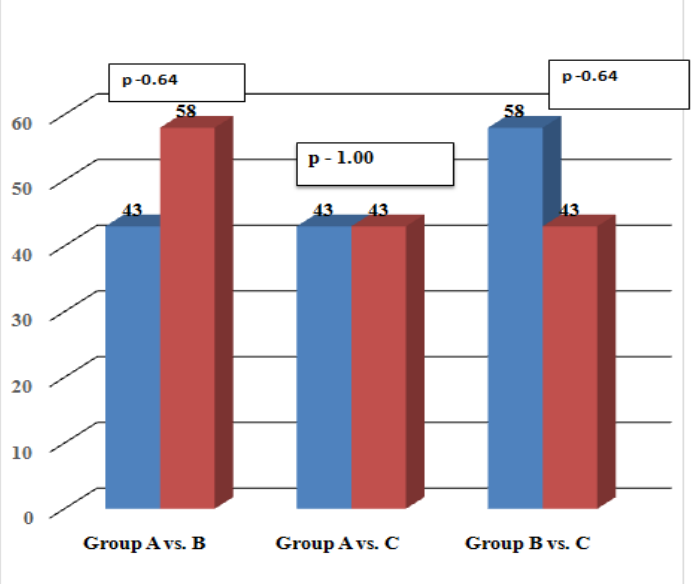
Table-4: Effects on lifestyle modification with DPP4 inhibitors on prediabetic subjects after the end of the study (Group C)

Variable	Baseline N=50	End of the study N=37	Mean change 95% Confidence interval	P value
BMI	24.0 ± 6.8	22 ± 3.8	3.6 (1.195 to 6.005)	**0.05**
Systolic blood pressure (mmHg)	123.8 ± 12.6	120 ± 12	3.00 (-1.76 to 7.76)	0.21
Diastolic blood pressure (mmHg)	78.1 ± 12.5	74 ± 12	4.00 (-0.76 to 8.76)	0.09
Fasting plasma glucose (mg/dl)	110 ± 12	101 ± 10	9.00 (4.62 to 13.38)	**0.0001**
2 hr after75gm glucose (mg/dl)	156 ± 24	132 ± 35	20.00 (-32.2363 to -7.7637)	**0.0001**
Serum Total Cholesterol (mg/dl)	212 ± 30	209 ± 34	3.00 (-9.73 to 15.73)	0.64
Serum Triglyceride (mg/dl)	156 ± 61	135 ± 32	21.00 (1.67 to 40.33)	**0.03**
Serum LDL (mg/dl)	93 ± 32	96 ± 28	-3.00 (-14.93 to 8.93)	0.62
Serum HDL (mg/dl)	47 ± 14	48 ± 12	-1.00 (-6.17 to 4.17)	0.70
HbA1c (%)	5.83±0.46	5.5 ± 0.44	0.310 (0.147 to 0.472)	**0.0004**
Incidence of diabetes	0/50	3(6%)	-	-
Reduction rate of DM		43%		

Note: Paired t test was done

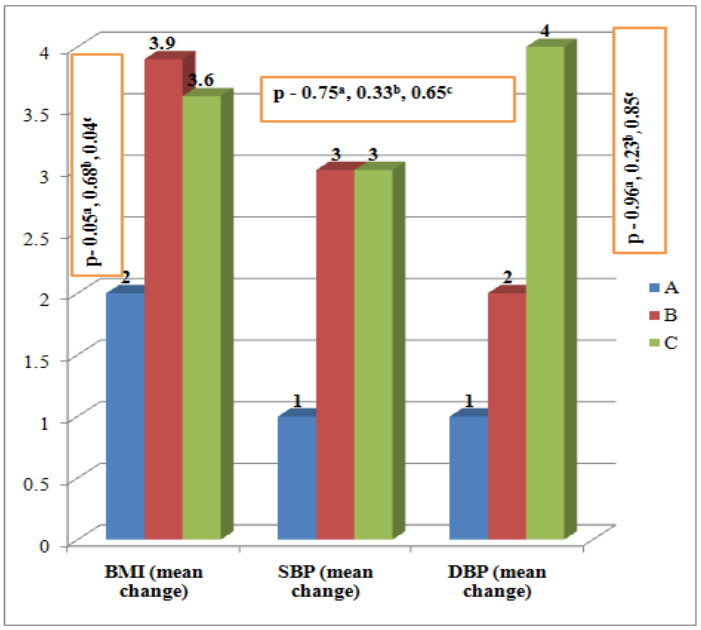
Table-4 shows that in Group C N=50 prediabetic subjects were advised for LSM+DPP4i, 37 were follow up at the end of study and found significantly change in BMI (p-0.05) Fasting (p-0.0001) & 2 hr plasma glucose level (p-0.0001) serum triglyceride level (p-0.03) and reduced HbA1c level (p-0.0004) respectively. The progress to diabetes is 6%and reduction rate of DM is 43%. There is no effect on systolic & diastolic blood pressure and also in HDL, LDL and total cholesterol level.

Figure1: Comparison of reduction difference of DM in percentage in between the group



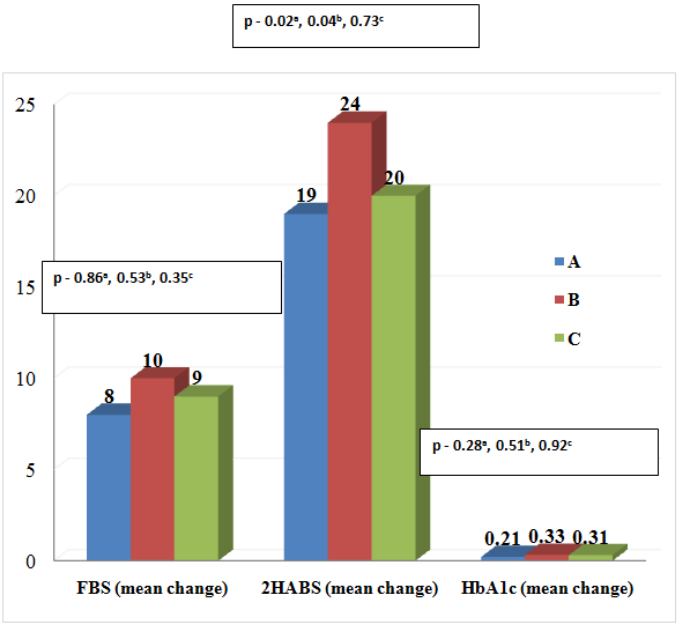
Note: Anova test was done.
Group A= LSM only, Group B= LSM + Metformin, Group C= LSM + DPP4i
Figure-1 shows that there is no significant outcome difference in reduction of diabetes in between the groups at the end of study.

Figure-2: Outcome difference in clinical parameters in between intervention group after the end of the study



Note: Anova test was done.
Group A= LSM only, Group B= LSM + Metformin, Group C= LSM + DPP4i
a p-value =A vs. B, b p-value = B vs. C, c p-value = A vs. C
Figure 2 shows that there is no significant outcome difference in BMI in between B & C group but outcome difference in between A vs B (p- 0.05) and A vs C group (p- 0.04). There is no significant outcome difference in SBP and DBP in between intervention group.

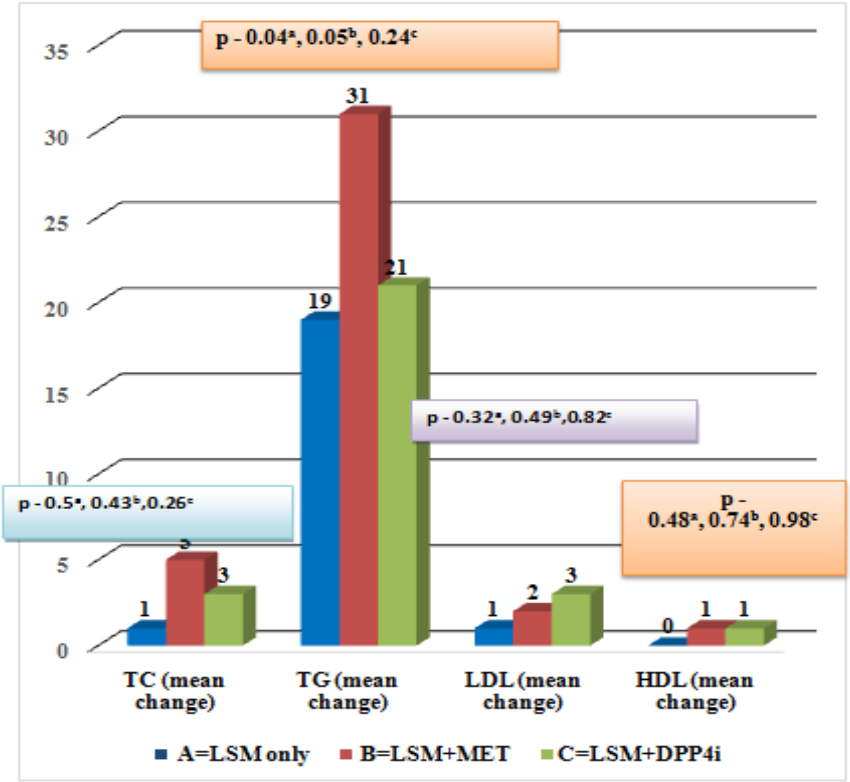
Figure-3: Outcome difference in glycemic profile in between intervention group after the end of the study



Note: Anova test was done.
Group A= LSM only, Group B= LSM + Metformin, Group C= LSM + DPP4i, a p-value =A vs. B, b p-value = B vs. C, c p-value = A vs. C

Figure-3 shows that there is no outcome difference in HbA1c and fasting blood sugar in between intervention group. But more mean changed in 2hrs after blood sugar level in lifestyle with metformin intervention group than lifestyle alone (p-0.02) and B vs. C group (p - 0.04). But mean changed in fasting blood sugar and 2 hrs after blood sugar, the outcome is same in between A and C group(p - 0.73).

Figure-4: Outcome difference in lipid profile in between intervention group after the end of the study



Note: Anova test was done.
a p-value =A vs. B, b p-value = B vs. C, c p-value = A vs. C
Figure-4 shows that there is no outcome difference in LDL, HDL and total cholesterol level in between intervention group but there is significant outcome difference in TG level in A vs. B (p - 0.04), B vs. C group (p - 0.05). There is no significant difference in TG level in A vs. C group.

IV. Discussion

Without intervention, prediabetes is likely to average time between onset and diagnosis of type 2 diabetes is 7 yr.[7] The aim of the study is to assess the clinical and biochemical profile of prediabetic subjects before and after lifestyle modification, metformin, and DPP-4 inhibitor and thus DM can be prevented in this high risk group. Drugs compliance are 84%, 88%, and 76% and drop out are 16%, 12%, and 26% in lifestyle only, lifestyle plus Metformin, and lifestyle plus DPP4i respectively. Mean drop out is 18% and most of them are due to non adherence to study protocol and drug adverse effect. In group A, 6(12%) did not follow the instruction for lifestyle modification and 3(6%) could not reach over telephone. In group B, 5(10%) complained about minor side effect and 1(2%) was not available on telephone. In group C, 9(18%) reported headache and 4(8%) told about diarrhea in the initial part of the study. After counseling other than the drop out, rest of the subjects continue the intervention. However there were not any serious adverse events. Our result shows the incidence of diabetes was reduced by 43 percent with the lifestyle intervention and by 58 percent with lifestyle plus metformin, 43 percent with lifestyle with DPP4 inhibitors. These effects were similar in men and women. The results from previous studies in Sweden[8] and China[9] also provide evidence that changes in lifestyle are effective in preventing diabetes, and the outcome in these studies was similar to that in our study. In those two studies, the subjects were not randomly assigned to the intervention and control groups. The randomization in our study was stratified according to the clinic, sex, and baseline plasma glucose concentration two hours after oral glucose challenge in order to obtain the best possible comparability between groups. In the Chinese study,[9] an attempt was done to determine whether a change in diet or a change in exercise habits was more effective, the study revealed no difference in outcome between the two interventions. We did not try to separate these changes but, rather, tried to achieve changes in lifestyle that were as extensive as possible for each subject in one group, another group was lifestyle with metformin and another one is lifestyle modification with DPP4 inhibitors. The effect of the interventions was assessed after one year because earlier assessment may be biased as a result of changes made only because subjects are conscious of being studied. The effect of the intervention on the incidence of diabetes was most pronounced among subjects who made comprehensive changes in lifestyle; on the other hand, the failure to make any changes resulted in an incidence of diabetes that was close to the

estimate of 35 percent for this high-risk population. The intensive lifestyle intervention was at least as effective in older participants as it was in younger participants. The results of our study extend previous data[10] showing that lifestyle interventions can reduce the incidence of diabetes and demonstrate the applicability of this finding to the ethnically and culturally diverse population of the United States. The risk reduction associated with the lifestyle intervention in our study was the same as that in a study conducted in Finland,[9] and was higher than the reductions associated with diet (31 percent), exercise (46 percent), and diet plus exercise (42 percent) in a study in China.[10] Our lifestyle intervention was systematic and intensive, with the study participants receiving detailed, individualized counseling. The study, however, was not designed to test the relative contributions of dietary changes, increased physical activity, and weight loss to the reduction in the risk of diabetes, and the effects of these components remain to be determined. The incidence of diabetes in our lifestyle group (6.0 cases per 100 person-years) was higher than we had anticipated 6 and was higher than the incidence in observational studies[11], perhaps owing to the greater frequency of glucose testing or to the selection of persons at higher risk in our study. The incidence of diabetes in the placebo group was similar among racial and ethnic groups despite differences in these subgroups in observational, population-based studies. Racial and ethnic group differences in the incidence of diabetes were presumably reduced in our study by the selection of persons who were overweight and had elevated fasting and post-load glucose concentrations — three of the strongest risk factors for diabetes. Previous studies have not demonstrated that drugs used to treat diabetes are effective for its prevention, perhaps because of small samples and the lack of data on adherence to the prescribed regimens. In contrast, metformin was effective in our study with lifestyle modification. The reduction in the average fasting plasma glucose concentration was similar in the lifestyle-intervention and metformin groups, but the lifestyle intervention with metformin had a greater effect than lifestyle with DPP4 inhibitors on glycosylated hemoglobin, and a larger proportion of participants in the lifestyle-intervention group had normal post-load glucose values at follow-up. These findings are consistent with[12] the observation that metformin suppresses endogenous glucose production, the main determinant of fasting plasma glucose concentrations. Rates of adverse events, hospitalization, and mortality were similar in the three groups, except that the rate of gastrointestinal symptoms was highest in the metformin group and the rate of musculoskeletal symptoms was highest in the lifestyle-intervention group. Thus, the interventions were safe in addition to being effective. An estimated 10 million persons in the United States resemble the participants in the Diabetes Prevention Program in terms of age, body-mass index, and glucose concentrations, according to data from the third National Health and Nutrition Examination Survey. If the study's interventions were implemented among these people, there would be a substantial reduction in the incidence of diabetes. Ultimately, the benefits would depend on whether glucose concentrations could be maintained at levels below those that are diagnostic of diabetes and whether the maintenance of these lower levels improved the long-term outcome. These questions should be addressed by continued follow-up of the study participants and by analysis of the main secondary outcomes; reductions in risk factors for cardiovascular disease, in the proportion of participants with atherosclerosis, and in the proportion with cardiovascular disease, which is the leading cause of death among patients with type 2 diabetes.[13] Optimal approaches to identifying candidates for preventive measures remain to be determined[14] although elevation of either the fasting or the post-load glucose concentration strongly predicts diabetes, both were required for eligibility in this study. Whether the results would be similar in persons with an isolated elevation of the fasting or post-load glucose concentration or other risk factors for diabetes is likely but unknown. The incidence of diabetes was same in lifestyle and life style with DPP4 inhibitors group that is 6% and lifestyle with metformin group the incidence is 4%. Outcome difference is some significant in between three intervention group. There is no significant outcome difference in BMI in between B & C group but outcome difference in between A vs. B (P value 0.05) and A vs. C group (P value 0.04). There is no significant outcome difference in SBP and DBP in between intervention group. No outcome difference in HbA1c and fasting blood sugar in between three intervention group. But more mean changed in 2hrs after blood sugar level in lifestyle with metformin intervention group than lifestyle alone (p value-0.02) and B vs. C group (p value-0.04). But Mean changed in fasting blood sugar and 2 hrs after blood sugar, the outcome is same in between A and C group (p value-0.73). There is no outcome difference in LDL, HDL and total cholesterol level in between intervention group but there is significant outcome difference in TG level in A vs. B (P value 0.04), B vs. C group (P value 0.05). There is no significant difference in TG level in Avs. C group. In our study incidence of diabetes in lifestyle intervention group was 6%, 4% in lifestyle plus metformin intervention group and 6% in lifestyle plus DPP4i intervention group. The reduction rate of diabetes 43% in lifestyle intervention group and 58% in lifestyle plus metformin intervention group and 43% also in lifestyle plus DPP4i intervention group. In DPP (diabetes prevention study) incidence of diabetes in control group was 11cases/ per 100, 7.8 cases/per 100 and 4.8 cases/100 in lifestyle intervention group. The reduction rate of diabetes 38% in lifestyle intervention group and 44% in lifestyle plus metformin intervention group. In DPPOS incidence of diabetes 5.9% in lifestyle intervention group and 4.9% in lifestyle plus metformin intervention group. The reduction rate of diabetes 34% in lifestyle intervention group and 52% in lifestyle plus metformin intervention group. A case report done by Johnson on prediabetic patient

with sitagliptin showed that after 18 months on sitagliptin, her A1C had improved to 5.8% without further lifestyle improvements from 6.4% and by 32 months, her A1C had improved to 5.6%. Her A1C was maintained within or below the prediabetes range of 5.7% to 6.4% over 3 years of treatment with sitagliptin. Sitagliptin may reduce beta cell apoptosis and preserve beta cell functioning, thereby preventing the progression from prediabetes to type 2 DM. In vitro studies suggest that activation of GIP and GLP-1 receptors promotes beta cell resistance to apoptosis, proliferation, and neogenesis, resulting in enhanced beta cell function. Our study showed that 43% reduction of diabetes on prediabetic patients after DPP4i with lifestyle intervention.

In summary, our study showed that treatment with metformin, DPP4 inhibitors and modification of lifestyle were highly effective means of preventing type 2 diabetes. The lifestyle intervention was particularly effective, with one case of diabetes prevented per seven persons treated for one year. Thus, it should also be possible to prevent the development of complications, substantially reducing the individual and public health burden of diabetes.

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